
Tahir Sultan Shamsi, Mohammad Irfan, Tasneem Farzana, Saqib Hussain Ansari, Ghazala Ahmad, Nazmeen Shakoor, Mirza Irfan Baig
Bismillah Taqee Institute of Health Sciences and Blood Diseases Centre, Karachi. Pakistan.

Abstract
The case report of a 2 year old boy with steroid refractory DBA, treated with allogeneic PBSCT from an HLA matched sibling is presented. Anti-IL2 receptor antibody Daclizumab was used as a prophylaxis for graft versus host disease (GvHD). Complete recovery without any evidence of GvHD ensued.

Introduction
Diamond Blackfan anaemia (DBA) is an early onset pure red cell aplasia characterized by macrocytosis, reticulocytopenia and marrow erythrolastopenia. Corticosteroid is the first line therapy in the treatment of Diamond Blackfan anaemia but 50% cases are steroid refractory; allogeneic PBSCT is a curative treatment.

Case Report
A 2 months old boy presented with features of severe anaemia. There was no family history of haemoglobinopathy or any other blood disorder. Laboratory investigations showed haemoglobin of 3.5gm/dl and slightly raised mean cell volume. Peripheral blood film showed normochromic and macrocytic RBC. Uncorrected reticulocyte count was 0.5%. Bone marrow biopsy exhibited marked erythrolastopenia in an otherwise normocellular marrow. A diagnosis of DBA was established. Oral prednisolone was started at 2 mg/kg/day for 6 months but there was no response to therapy, and patient remained transfusion dependent. Parents were counselled for allogeneic PBSCT. His elder brother was HLA identical; transplant was done when the child was 20 months old. Conditioning therapy consisted of oral Busulphan 3.5 mg/kg body weight/day for 4 days and injection Cyclophosphamide 50 mg/kg/day for 4 days. Donor stem cells were mobilized with subcutaneous rhG-CSF at a dose of 10 g/kg/day for 4 days and on day 0 stem cells were harvested using MCS+ cell separator (Haemonetics USA). The dose of mononuclear cells was 6.2x10^8/kg body weight of the recipient. Acute GvHD prophylaxis given in a form of oral Cyclosporin 5 mg/kg/day started from day-4, oral Methotrexate 10 mg/m² on day +1, 3, 6, 11 and then weekly. Interleukin 2 receptor blocking antibody Daclizumab was given on day 0. This regimen was well tolerated by the patient. Patient developed febrile neutropenia on day +4 which responded to empirical antibiotics. The platelets never dropped below 20 x 10^9/L. Neutrophils were engrafted on day +9. Patient was discharged from hospital on day +19. Immunosuppressive therapy was withdrawn gradually after six months. Patient has been in excellent clinical condition 2 ½ years post transplant, maintaining his haemoglobin with normal haematopoiesis. Details of peripheral blood counts and engraftment are given in Table.

Table. Details of blood count and engraftment.

<table>
<thead>
<tr>
<th>Blood Count</th>
<th>Days after stem cell infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Hb (gm/dl)</td>
<td>10.5</td>
</tr>
<tr>
<td>WBC (x10^9/l)</td>
<td>3.7</td>
</tr>
<tr>
<td>Neut (x10^9/l)</td>
<td>1.9</td>
</tr>
<tr>
<td>Plat (x10^9/l)</td>
<td>316</td>
</tr>
</tbody>
</table>

Hb: haemoglobin; WBC: white blood cells; Neut: neutrophil; Plat: Platelet.

Discussion
Efficacy of Daclizumab as a prophylaxis of GvHD has not been tested in DBA or other indications. Response rates of 29% and 47% have been reported in steroid resistant acute GvHD, using two different time schedules of antibody administration respectively.1,2 In this case of steroid refractory DBA, Daclizumab proved useful in preventing acute GvHD and cGvHD. This was the first case of DBA which received Daclizumab in allogeneic PBSCT and recovered completely. Acute graft versus host disease is one of the most common causes of transplant related mortality. Cyclosporin, Methotrexate and steroids are used for its prophylaxis but once it develops it has significant morbidity and mortality. Anti-thymocyte globulin (ATG) and more recently, anti-IL2 receptor antibodies Daclizumab have been used in steroid refractory acute GvHD for its treatment. Although ATG is in use for matched unrelated donor transplant GvHD prophylaxis, Daclizumab has not been tried in this setting.

First successful bone marrow transplant in DBA was reported in 1976 in a 13 year old boy.3 The patient died due
to interstitial pneumonia on day +55 but the haematopoietic engraftment confirmed that the DBA is a transplantable disorder. Since then over a hundred bone marrow transplants have been reported in literature. International bone marrow transplant registry, French registry and DBA registry reported a series of 10, 13 and 20 patients respectively.4-7 In HLA identical sibling donor transplant, 72-87.5% 2 year or a 5 year probability of survival was seen while in unrelated matched setting the outcome was extremely poor. Main causes of transplant failure were acute GvHD, relapse of DBA and infections.

**Conclusion**

In steroid refractory DBA, we suggest an early decision of transplant before iron overload induced end-organ damage and transfusion transmitted viral infections complicate the picture. Newer approaches of prevention of GvHD e.g. Daclizumab need to be tested to improve the outcome of allogeneic PBSCT.

**References**